EXHIBIT 1

Based on my review of the reliable and credible publicly available published peer-reviewed scientific literature regarding calcium nutrition, metabolism, and physiology, their interactions with skeletal physiology, and the disease-preventing properties of dietary calcium in the prevention of bone fractures, I conclude that there is significant scientific agreement in support of the following health claims:

- Calcium may reduce the risk of bone fractures.
- Calcium may reduce the risk of hip fractures.
- Calcium may reduce the risk of vertebral fractures.
- Calcium may reduce the risk of wrist fractures.
- Calcium may reduce the risk of nonvertebral fractures.

Calcium

I. Intestinal Calcium Absorption and Retention of Ingested Calcium

A. Mechanisms of Calcium Absorption

Calcium in foods occurs as salts or in association with other dietary constituents in the form of complexes of calcium ions. Calcium must be released in a soluble, and probably ionized, form before it can be absorbed (i.e., transferred from the intestinal lumen to the circulatory system). Once in a soluble form, calcium is absorbed by two routes, transcellular and paracellular transport.[1]

The saturable, transcellular pathway is a multi-step process, involving the entry of luminal calcium ions across the microvillar membrane into the enterocyte, then movement through the cytosol (i.e., translocation to the basolateral membrane), followed by active extrusion from the enterocyte into the lamina propria and diffusion into the general circulation. The entry of calcium ions across the apical membrane of the enterocyte is favored electrochemically because the concentration of calcium ions within the cell (10^{-7} to 10^{-6} M) is considerably lower than that in the intestinal lumen (10^{-3} M), and the cell is electronegative relative to the intestinal lumen.[1] Therefore, the movement of calcium ions across the apical membrane does not require the expenditure of energy. However, because lipid membranes are impermeable to calcium ions, apical entry must involve the participation of a calcium ion channel or integral membrane transporter residing within the brush border membrane. Evidence suggests that the calcium transport protein, CaT1, may be the putative calcium ion transporter.[2,3]

The intracellular diffusion of calcium ions is thought to be facilitated by a cytosolic calcium-binding protein, calbindin D_{9K}, whose biosynthesis is dependent on the presence

of vitamin D (in the form of 1,25-dihydroxycholecalciferol). Calbindin D_{9K} facilitates the diffusion of calcium ions across the cell by acting as an intracellular calcium ferry or chaperone. The active extrusion of calcium ions at the basolateral membrane takes place against an electrochemical gradient and is mediated primarily by a calcium-dependent ATPase. While each step in the transcellular movement of calcium ions has a vitamin D-dependent component, the intracellular concentration of active calbindin D_{9K} is believed to be rate-limiting in 1,25-dihydroxycholecalciferol-induced transcellular calcium transport.[1]

The paracellular route of calcium absorption involves passive calcium transport through the tight junctions between mucosal cells. Because it does not require a transporter and is driven by the large luminal:serosal calcium concentration gradient, this transport pathway is non-saturable and appears to be independent of nutritional or physiologic regulation (although some limited evidence suggests that it also may respond to 1,25-dihydroxycholecalciferol in an as yet unknown manner).[1,4]

Most calcium absorption in humans occurs in the lower small intestine, but there is some evidence for a colonic component that may increase total calcium absorption by as much as 10%.[5] However, the large intestine may represent a site of increased importance for calcium absorption when acidic fermentation takes place. Slightly acidic intracolonic pH increases the efficiency of colonic absorption of calcium.[6] For example, prebiotics acidify slightly the intracolonic pH (secondary to increased production of short-chain fatty acids as byproducts of increased fermentation) and have been shown to increase the fractional true absorption of ingested calcium in human adolescents, young adults and postmenopausal women.[6]

When dietary calcium is abundant, the paracellular pathway appears to be dominant.[7] When dietary calcium is limited, the active 1,25-dihydroxycholecalciferol-dependent transcellular pathway increases in importance.[7] Transmembrane calcium receptors (especially in renal tissues) mediate the conversion of 25-hydroxycholecalciferol to biologically-active 1,25-dihydroxycholecalciferol through regulation of the expression of 25-hydroxycholecalciferol-1α-hydroxylase and thereby indirectly regulate hormone-mediated up-regulation and down-regulation of calbindin D_{9K} activity in mucosal cells.[1] The beginning of a decline in plasma calcium ion concentration evokes an increase in serum 1,25-dihydroxycholecalciferol concentration, which in turn stimulates increased calbindin D_{9K} biosynthesis in the intestinal mucosa.[1]

B. Efficiency of Calcium Absorption

The efficiency of absorption of ingested calcium is inversely proportional to chronic calcium intake. However, this adaptive decrease in the fraction of ingested calcium that does not appear in the feces as calcium intake decreases is not sufficient to offset the decrease in the amount of calcium that is absorbed as a result of a decrease in calcium intake.[8,9] Regardless of the efficiency of absorption, the amount of calcium that is

absorbed is directly proportional to the amount ingested.[8,9] For example, despite the significantly greater efficiency of absorption when human calcium intake is less than 500 mg/day, the total amount of calcium absorbed from such a low-calcium diet is less than half the amount that is absorbed (even with significantly lower efficiency) from a diet providing 1000 mg/day.[10,11]

The efficiency of calcium absorption varies throughout the life cycle. It is greatest in infancy, when about 60% of consumed calcium is absorbed,[12] decreases during childhood, and increases again early in adolescence, when about 25% of consumed calcium is absorbed.[13] The efficiency of calcium absorption remains at about this level into middle adulthood.[13] As adults age beyond middle adulthood, the efficiency of calcium absorption declines gradually. For example, in postmenopausal women and older men, the efficiency of calcium absorption has been reported to decrease by an average of about 0.2 percentage points annually.[13,14]

Decreased production of estrogen results in decreased efficiency of calcium absorption in women at any age.[8,13] For example, the apparent absorption of dietary calcium by premenopausal and perimenopausal women ranges between 17% and 58% and decreases slightly with increasing calcium intake.[15] However, women over 65 years old respond to low calcium intakes with significantly smaller increases in fractional calcium absorption than occur in women 20 to 35 years old consuming the same inadequate amount of calcium.[16] Similarly, amenorrheic young women with hypoestrogenic anorexia nervosa have significantly less efficient calcium absorption than is enjoyed by healthy eumenorrheic young women.[17]

Racial differences affect the efficiency of calcium absorption. For example, African American girls exhibit significantly more efficient calcium absorption after menarche than do Caucasian girls.[18] Interestingly, African American adults later exhibit significantly lower rates of bone fractures than do Caucasian adults.[19,20]

C. Calcium Retention

The retention of ingested calcium within the body reflects the interplay among the amount of calcium consumed, the efficiency of calcium absorption, and urinary excretion of calcium. For example, when a group of healthy adult women reduced their calcium intake from 2000 mg/day to 300 mg/day, although their efficiency of calcium absorption increased significantly, their urinary excretion of calcium decreased significantly, and their efficiency of whole body retention of ingested calcium increased significantly (from 27% to 37%), the overall net result was a significant decrease in the net amount of calcium retained (from 540 mg/day to 111 mg/day).[21]

Amenorrheic young women with anorexia nervosa have significantly greater urinary excretion of calcium than healthy eumenorrheic women; coupled with the reduced absorption efficiency also exhibited by such women, these greater losses produce

significantly reduced net calcium retention (evidenced by significantly reduced bone mass).[17] Similarly, in contrast to the generally beneficial effects of moderate exercise on calcium metabolism and skeletal physiology, exercise-induced amenorrhea also produces significantly decreased net calcium retention (and lower bone mass).[22,23]

Vegetarian diets produce metabolizable anions (such as acetate and bicarbonate) that may increase renal resorption of filtered calcium, decreasing urinary calcium excretion.[24,25] Consequently, vegetarians may be more efficient retainers of dietary calcium.

Racial differences may affect the efficiency of calcium resorption in the kidneys. For example, African American children aged 9 to 18 years have exhibited significantly less urinary excretion of calcium than similarly-aged Caucasian children.[26] In contrast, it was reported that less calcium was excreted in the urine of African American girls before menarche but that urinary calcium excretion was similar in African American and Caucasian girls after menarche.[18]

Data from 181 balance studies subjected to nonlinear regression analysis indicate that maximal calcium retention occurs in men and women when dietary calcium intake is 1200 mg/day.[27-29] Nonetheless, this level of intake may be inadequate for many individuals. For example, a daily intake of 1300 mg of calcium was insufficient to maximize calcium retention in all members of a group of adolescent females.[28]

II. Bone Fractures

A. Rate and Risk of Bone Fractures

The number of new hip fractures occurring worldwide is expected to exceed 6 million annually by 2050.[30] The National Osteoporosis Foundation estimates that over 1.5 million fractures associated with chronic calcium deficiency occur in the US annually (700,000 vertebral fractures, 300,000 hip fractures, 250,000 wrist fractures, and 300,000 other fractures), with daily treatment costs in excess of $40 million.[31] For a 50-year-old Caucasian woman, the risk of sustaining a hip fracture during the next 30 years is about 17%.[32]

Hip fractures in elderly patients result in substantial morbidity and mortality.[33] Most patients fail to regain their previous level of functional competence.[34] Up to 20% of hip fracture victims require permanent institutionalization.[34,35] The risk for dying increases 2- to 10-fold during the first year after a hip fracture.[36,37] About 25% of deaths during the first year after a hip fracture are directly related to the hip fracture.[38] Fewer than 80% of patients sustaining a proximal femoral fracture survive the first year following the fracture.[39] The incidence of hip fractures in men is about half that in women but because they occur in men on average about ten years later in life, they carry about twice the risk

for fracture-associated death.[39-41] Similarly, vertebral fractures are associated with increased risk for premature death (relative risk (RR) for dying from a vertebral fracture: 1.23; 95% confidence interval (CI): 1.10, 1.37;[42] RR: 1.23; 95% CI: 1.09, 1.43;[43] RR: 1.92; 95% CI: 1.70, 2.14[44]).

In women, the rate of hip fracture doubles about every 5 years after age 40.[45] If preventive nutrition could delay the onset of fracture by an average of five years, the rate of hip fracture in women could be reduced by almost 50%.[45]

The two main determinants of hip fracture risk are falls and a reduction in bone mass, particularly of cortical bone mass leading to increased bone fragility.[46-52] Increased bone fragility may be caused by several factors: (1) submaximal peak bone mass at maturity; (2) the slow age-related bone loss occurring in adults of both sexes; (3) the accelerated postmenopausal bone loss occurring in women; and (4) the secondary hyperparathyroidism that produces osteoporosis.[50]

Age-related bone loss occurs throughout life, even in the very elderly, and involves both cortical and trabecular bones.[53] Factors associated with aging contribute to this slow steady loss.[53] Decreased intestinal absorption of calcium independently increases the risk for hip fracture; in a prospective observational study (the "Study of Osteoporotic Fractures"), the age-adjusted risk for hip fracture increased by 24% for every 7.7% decrease in fractional intestinal absorption of dietary calcium.[54] Among women with daily calcium intakes less than 400 mg, the age-adjusted risk for hip fracture for women with fractional intestinal absorption of dietary calcium less than 32.3% was significantly greater than that of women with fractional intestinal absorption of dietary calcium greater than 32.3% (RR: 2.46; 95% CI: 1.29, 4.69).[54]

Secondary hyperparathyroidism contributes to the risk of hip fracture through acceleration of bone resorption.[53] Inadequate calcium intake in the face of accelerated bone remodeling produce a negative calcium balance, with a reduction in plasma ionized calcium concentration that stimulates secretion of resorption-inducing parathyroid hormone (PTH) by the parathyroid gland.[53] By causing dysequilibrium in bone remodeling in favor of net resorption, secondary hyperparathyroidism (secondary to dietary calcium inadequacy) produces cortical bone loss (although remaining bone tissue is mineralized normally; "osteoporosis") and increases the risk of hip fractures.[55-57] Patients with recent hip fractures exhibit greater circulating PTH concentrations than do age-matched unfractured control subjects.[55,58] In a randomized placebo-controlled clinical trial comparing placebo to daily dietary supplementation with calcium (1600 mg as calcium citrate) for 4 years in postmenopausal women, supplementation produced a significantly greater decrease in serum PTH concentration.[59] Similarly, in elderly women, daily supplementation with 2400 mg of elemental calcium significantly reduced serum parathyroid hormone concentrations, resulting in serum parathyroid hormone concentrations typical of young adult women.[60] In a randomized placebo-controlled clinical trial comparing placebo to daily dietary supplementation with calcium (1200 mg)

plus vitamin D (800 IU) for 2 years in women aged 64 to 99 years, supplementation produced a significantly greater decrease in serum parathyroid hormone concentrations.[61] In contrast, hip fractures not preceded by chronic secondary hyperparathyroidism comprise less than 10% of all hip fractures.[55-57,62]

B. Dietary Calcium and Bone Fractures

In three randomized placebo-controlled clinical trials, dietary supplementation with calcium has significantly reduced the incidence of new fractures.[63-65] Elderly postmenopausal women without prevalent fractures responded to daily dietary supplementation with 1000 mg of calcium (as calcium carbonate) with significantly greater reduction in the incidence of new spinal and hip fractures during the 4 years of the trial, compared to the effect of placebo.[63] Similarly, elderly postmenopausal women with histories of spinal fractures and consuming less than 1000 mg of calcium daily prior to the trial responded to daily dietary supplementation with 1200 mg of calcium (as calcium carbonate) with a 77% reduction in the incidence of new spinal fractures during the 4 years of this trial (a significantly greater reduction than the reduction attributable to placebo).[64] In a randomized placebo-controlled study of women who previously had suffered multiple fractures, daily dietary supplementation with 1500 to 2500 mg of calcium (as calcium carbonate) produced a significantly greater reduction in the incidence of new fractures.[65] In contrast to these reports, daily dietary supplementation with either 750 mg,[66] 800 mg[67] or 1600 mg[59] of calcium had no greater effect than placebo on the incidence of hip fractures in men or women. However, in two of these studies, daily dietary supplementation with calcium was insufficient to prevent calcium deficiency in about half of the supplemented subjects.[66,67]

In two other randomized placebo-controlled clinical trials, dietary supplementation with calcium in combination with vitamin D has significantly reduced the incidence of new fractures.[68-70] In a randomized comparison of placebo to daily dietary supplementation with calcium (1200 mg) plus vitamin D (800 IU) in healthy elderly women 69 to 106 years old with a mean prestudy daily dietary calcium intake of 500 mg, supplementation for 18 months significantly reduced the risk for new nonvertebral fractures by 75% (RR: 0.25; 95% CI: 0.09,0.38) and significantly reduced the risk specifically for new hip fractures by 74%.[68] These decreases were sustained during the second 18 months of the study (after 36 months: hip fractures: RR: 0.73; 95% CI: 0.67, 0.84; all nonvertebral fractures: RR: 0.72; 95% CI: 0.60, 0.84).[69] In another randomized placebo-controlled clinical trial, supplemental calcium (500 mg/day) plus supplemental vitamin D (700 IU/day) for 3 years halved the risk for new nonvertebral fractures in women over 65 years old (RR: 0.54; 95% CI: 0.12, 0.77) and in adult men (RR: 0.4; 95% CI: 0.2, 0.8).[70] In contrast, in one randomized placebo-controlled clinical trial comparing placebo to daily dietary supplementation with calcium (1200 mg) plus vitamin D (800 IU) for 2 years in women aged 64 to 99 years, the risk for hip fracture was not affected by dietary supplementation (RR: 1.69; 95% CI: 0.96, 3.0).[60] In one randomized clinical trial in which daily dietary calcium supplementation (1200 mg of elemental calcium as calcium

carbonate) was compared to daily dietary supplementation with calcium (1200 mg) plus vitamin D (800 IU daily), supplementation with calcium failed to affect the rate of falls in very elderly institutionalized women (mean age: 85 years) during a 3-month period, although combined supplementation significantly reduced the rate of falls by 49% (no data were presented concerning fractures).[71]

Indirect evidence for the fracture-preventing properties of dietary supplementation with calcium was provided by an uncontrolled study in which 1000 g of elemental calcium in unspecified form daily was equivalent to both alendronate and calcitonin in the prevention of new vertebral fractures among a group of postmenopausal women.[72] In another uncontrolled study, a group of postmenopausal and premenopausal women consuming supplemental calcium (1200 to 2000 g of elemental calcium as calcium lactate gluconate daily) exhibited no reduction in their presupplementation rate of new vertebral fractures during the 4.3 years of the study, although the expected aging-related increase in fracture rate[45] was prevented by dietary supplementation with calcium lactate gluconate.[73] In a study "controlled" by withholding any intervention from some of the subjects, daily dietary supplementation with 500 mg of calcium for 9 weeks had no effect on the incidence of stress fractures in healthy young male military recruits during an intense physical training program.[74]

In a prospective epidemiologic study, men suffering forearm or wrist fractures consumed significantly less dietary calcium than did men without such fractures (virtually none of the men suffering such fractures consumed 1200 mg of calcium daily).[51] However, mean dietary calcium intakes of men with and without humeral fractures were not different nor were the daily calcium intakes of women with or without humeral, forearm or wrist fractures.[51] In this study, fewer than 5% of all subjects consumed 1200 mg of calcium daily.[51]

Two prospective epidemiologic studies have found that the risk for fractures was significantly decreased by routine consumption of less inadequate amounts of dietary calcium.[75,76] In a 5-year prospective observational study of 11,798 perimenopausal and postmenopausal women, the risk for distal forearm fracture was nearly halved by consumption of over 1000 mg of calcium daily compared to the effect on the risk for distal forearm fracture of daily consumption of less than 500 mg of calcium (adjusted RR: 0.61; 95% CI: 0.43, 0.85).[75] In a 14-year prospective observational study, the risk for hip fracture was found to be significantly reduced (by 60%) in women consuming more than 765 mg of calcium daily compared to the risk in women consuming less than 470 mg of calcium daily (RR: 0.4).[76] For every 200 mg increment of daily dietary calcium intake greater than 600 mg/day, the risk for hip fracture decreased by about 40%.[76] Using this estimate, a daily intake of 1200 mg could cut fracture risk among the general population by about 75%,[76] a decrease in risk similar to those achieved in randomized placebo-controlled clinical trials.

Other observational studies failed to report a statistically significant association between dietary calcium intake and bone fractures.[49,77-84] However, the study populations in these reports were almost universally calcium deficient (some severely so), suggesting that a finding of no association between dietary calcium intake and bone fractures applies only to chronically calcium deficient individuals, whose daily calcium intakes are well short of current Institute of Medicine recommendations.[29] Furthermore, consistent with the conclusion that the consumption of at least 1200 mg of dietary calcium daily is required to maximize net calcium retention[27-29] and with the daily dietary calcium intakes achieved with supplementation in the randomized placebo-controlled clinical trials in which dietary supplementation with calcium significantly reduced the incidence of fractures (between 1000 and 2500 mg daily,[63-65] while 750[66] or 800[67] mg daily were ineffective), these studies[49,77-84] support the conclusion that there is a similar threshold of dietary calcium intake required to trigger a statistically significant reduction of fracture risk.

For example, in a prospective observational study (the OFELY Study), healthy postmenopausal women experiencing hip fractures had a mean daily dietary calcium intake of 824 mg compared to a mean daily intake of 804 mg by women who did not experience a fracture during the 5 years of the study; however, fewer than 15% of the women experiencing hip fractures and fewer than 15% of the women who did not experience a fracture during the 5 years of the study consumed at least 1200 mg of calcium daily.[49] In a 3-to-6-year observational study of 3,068 women, dietary calcium intake had no effect on the risk for bone fractures, although fewer than 5% of these women consumed more than 800 mg of calcium daily and virtually none consumed 1200 mg or more of calcium daily.[77] In the prospective observational NHANES I Epidemiologic Follow-Up Study of 4342 men and women who were aged 50 to 74 years at the beginning of the study and who were observed for up to 16 years, daily dietary calcium intake had no effect on the incidence of hip fracture; however, fewer than 5% of these subjects consumed at least 1200 mg of calcium daily.[78] In a cohort of 2879 white men aged 45 to 74 years and observed for up to 22 years (a subgroup of the NHANES I Epidemiologic Follow-Up Study), risk for hip fracture was independent of dietary calcium intake; however, fewer than 5% of these subjects consumed at least 1200 mg of calcium daily.[79] In the 8-year prospective Health Professionals Follow-Up Study of 43,063 men aged 40 to 75 years, the risks for both hip fracture and forearm fracture were found to be independent of daily calcium intake; however, only about 20% of these subjects consumed over 1200 mg daily.[80] In a prospective observational study of 72,337 postmenopausal women observed for 18 years (the Nurses' Health Study), the risk for hip fracture for women with daily calcium intakes greater than 1200 mg was not different from the risk for women consuming less than 600 mg daily (age-adjusted OR: 0.96; 95% CI: 0.68, 1.34).[81] However, excluding women who began consuming calcium supplements during the study, fewer than 10% of the study participants consumed at least 1200 mg of calcium daily.[81] In addition, only about 25% of the study participants began consuming calcium supplements during the study.[81] In a prospective observational study of 60,689 premenopausal and postmenopausal women observed for an average of 11.1

years (the Swedish Mammography Screening Cohort), the risk for hip fracture for women with daily calcium intakes greater than 1200 mg was not different from the risk for women consuming less than 400 mg daily (age-adjusted RR: 1.00; 95% CI: 0.79, 1.27); however, fewer than 10% of the study participants consumed at least 1200 mg of calcium daily.[82]

Although the results of two other prospective observational studies support the conclusion that subthreshold calcium intakes fail to reduce the incidence of new fractures, estimates of the percentages of study subjects consuming at least 1200 mg of calcium daily could not be determined from the data presented.[83,84] In an 11-year prospective observational study of adult men and women, the risk for hip fracture was found to be independent of total daily dietary calcium intake; however, only about 25% of these subjects consumed more than 718 mg of calcium daily.[83] In the other study, the incidence of hip fracture was found to be independent of dietary calcium intake, although fewer than one-third of the women in this study consumed more than 800 mg of calcium daily and fewer than 33% of the men consumed more than 1000 mg daily.[84]

Additional support for the conclusion that there is a threshold of dietary calcium intake required to maximize the reduction of fracture risk is provided by the results of three prospective epidemiologic studies in which the risk for fractures differed among subcohorts of chronically calcium deficient study subjects.[85-88] In an 18-year prospective observational study of 77,761 women aged 34 to 59 years at the beginning of the study, none of whom ever consumed calcium supplements, after 12 years, the risk for hip fracture was significantly increased among women with daily dietary calcium intakes greater than 900 mg compared to that for women with daily dietary calcium intakes below 450 mg (RR: 2.04; 95% CI: 1.12, 3.71).[85] In a prospective observational cohort study of women 65 years or older at baseline, the risks for fractures of the hip, ankle, proximal humerus, wrist or vertebrae were found to be independent of total daily calcium intake; in contrast, any calcium supplementation was found to significantly increase the risks for hip fracture (RR, calcium supplementation compared to no supplementation: 1.5; 95% CI: 1.1, 2.0) and for vertebral fracture (RR, calcium supplementation compared to no supplementation: 1.4; 95% CI: 1.1, 1.9).[86,87] However, even with supplementation, only 13% of these women consumed at least 1200 mg of calcium daily. In addition, according to these investigators, although these data suggest that the use of calcium supplements may increase the risk for fracture, this finding probably is an artefact of their study design, in which individuals at high risk for fractures were the most likely to have begun taking calcium supplements prior to or during the study.[86,87] In another prospective observational study of 8600 postmenopausal women and 5049 retired men, risk for hip fracture was not significantly affected by calcium intake, whether from foods or supplements; unfortunately, the percentage of study subjects consuming at least 1200 mg of calcium daily cannot be determined from the data presented.[88]

Retrospective epidemiologic studies also have found that the risk for fractures was significantly decreased by routine consumption of adequate amounts of dietary calcium.[86-103] In a retrospective observational case-control study, men with hip fractures

consumed significantly less calcium than did age-matched fracture-free subjects.[89] In another retrospective case-control study (the Asian Osteoporosis Study), the prevalence of hip fractures was not related to daily calcium in men; however, among women, the mean calcium intake of those sustaining hip fractures was significantly lower than that of those who were fracture-free.[90] In a comparative cross-sectional study of 2 geographically-distinct cohorts of postmenopausal women in Italy that were significantly different in their daily calcium intakes, the cohort of women with significantly greater daily calcium intakes experienced significantly fewer fractures of all sites.[91] In a cross-sectional case-control study of men and women aged 45 years and older, subjects without fractures consumed significantly more calcium (576 mg/day compare to 490 mg/day; $p<0.01$).[92] In two other retrospective case-control studies it was found that the prevalence of hip fracture[93] and vertebral fracture[94] were significantly inversely proportional to daily dietary calcium intake.

In a retrospective case-control study of women over 50 years of age, routine consumption of calcium supplements significantly reduced the risk for hip fracture (adjusted RR: 0.75; 95% CI: 0.60, 0.94).[95] In a retrospective case-control study of elderly men and women, the daily consumption of over 500 mg of calcium significantly reduced the risk for all fractures by 72% (OR: 0.28) compared to the risk among those subjects consuming less than 500 mg of calcium daily.[96] In a similar study, the incidence of hip fracture was independent of total daily dietary calcium intake in women but was significantly reduced by 84% (RR: 0.16; 95% CI: 0.03, 0.77) in men consuming over 1000 mg of calcium daily (compared to men consuming less than 500 mg of calcium daily).[97] In a case-control study of postmenopausal women, the risk for Colles' fractures was significantly decreased by 63% (OR: 0.37; 95% CI: 0.16, 0.85) in women consuming more than 1000 mg of dietary calcium daily (compared to women consuming less than 300 mg/day).[98] In another case-control study of postmenopausal women, subjects voluntarily consuming any calcium-containing dietary supplements for at least 5 years exhibited significantly reduced risk for hip fracture.[99] In another case-control study of postmenopausal women, subjects having suffered a hip fracture exhibited significantly lower serum total calcium concentrations than did unfractured women.[100]

In a subgroup of a retrospective observational case-control study (the MEDOS study), the risk for hip fracture was significantly decreased among women over 50 years old consuming the highest quartile of milk consumption, compared to the risk experienced by women over 50 years old consuming the lowest quartile of milk consumption (RR: 0.77; 95% CI: 0.66, 0.89).[101] Furthermore, the risk for hip fracture in women consuming the highest quintile of daily calcium intake was significantly less than that of women consuming the lowest quintile of daily calcium intake (RR: 0.4; 95% CI: 0.2, 0.8).[102,103] However, the incidence of hip fracture in men was not affected by milk intake in the MEDOS study.[104]

Epidemiologic data on women over 50 years old taken from the NHANES III database indicate that the risk for fractures was significantly halved (OR: 0.50; 95% CI: 0.38,

0.89) for women with milk intake prior to 13 years old of more than one serving daily, compared to the risk calculated for women with milk intake prior to 13 years old of less than one serving per week (one serving of milk provides about 300 mg of calcium).[105] The rate of bone fractures in adolescent children was found to be inversely proportional to their intake of calcium from drinking water.[106] Among adolescent girls, the risk for bone fractures was significantly reduced (by about 2/3; OR: 0.29; 95% CI: 0.11, 0.78) when daily calcium intake exceeded 1200 mg, although the risk for bone fractures appeared to be independent of daily calcium intake in adolescent boys.[107] In two retrospective epidemiologic studies, it was reported that the risks for hip fracture[108] or stress fracture[109] for adult women were independent of estimated calcium intakes during adolescence.

Other retrospective observational case-control studies provide additional support for the conclusion that there is a threshold of dietary calcium intake required to maximize the reduction of fracture risk.[110,111] For example, a retrospective observational case-control study found no relationship between dietary calcium intake and the risk for hip fracture among women 50 to 84 years old with daily calcium intakes less than 1200 mg.[110] In another case-control study, the risk for hip fracture was reported to be independent of either total or supplemental calcium intake among adult men and women with daily total calcium intakes less than 1200 mg.[111]

Although the results of six other retrospective observational studies support the conclusion that inadequate calcium intakes fail to reduce the incidence of new fractures, estimates of the percentages of study subjects consuming at least 1200 mg of calcium daily could not be determined from the data presented.[112-117] In a case-control study (the Multiple Risk Survey on Swedish Women for Early Assessment), the risk for hip fracture in women was found to be independent of total daily dietary calcium intake; however, only about 25% of these subjects consumed more than 1000 mg of calcium daily.[112] In a case-control study of women with and without hip fracture, there was no effect of dietary calcium intake on risk for fracture; however, fewer than 20% of the subjects consumed over 1026 mg of calcium daily.[113] In a cross-sectional study of women aged 19 to 25 years, lifetime history of fractures was unaffected by calcium intakes reported at the time of the study; however, the percentages of subjects consuming at least 1200 mg of calcium daily cannot be determined from the data presented.[114] In three other studies the risk for hip fractures was not affected by calcium intakes, but the percentages of subjects consuming at least 1200 mg of calcium daily cannot be determined from the data presented.[115-117]

A meta-analysis of 3 randomized placebo-controlled clinical trials calculated estimated pooled relative risks for hip fracture of 0.53 (95% CI: 0.31,0.90) and all nonvertebral fractures of 0.61 (95% CI: 0.46,0.80) among women consuming 500 to 1200 mg/day of supplemental calcium for 3 years or more.[118] These estimated relative risk ratios with their 95% confidence limits indicate that dietary supplementation with calcium possesses a significant fracture risk-lowering capability. Other investigators performing a

comprehensive review concluded that daily supplementation with 1300 to 1700 mg of elemental calcium significantly reduced the risk of fractures in the elderly.[119] The results of a systematic review of studies on elderly subjects concluded that daily dietary supplementation with calcium (1200 to 2500 mg for 3 to 5 years) produced significant reductions in risk of approximately 50% for vertebral fractures (although this analysis included one study[120] with an outcome of radiographically evident vertebral deformation rather than clinical gross fracture).[121] Investigators conducting a systematic review (published in 2002) concluded that "Ca^{2+} and vitamin D supplements at the dosage of 1000 – 1500 mg of elemental Ca^{2+} and 600 – 800 IU of vitamin D_3 daily assure in a population at risk for deficiencies…the decrease in the incidence of hip fractures and other non-vertebral fractures."[122] Investigators conducting a meta-analysis of published clinical trials concluded that daily dietary supplementation with 500 to 1200 mg calcium significantly reduced the risk for vertebral fracture by about 35% (RR: 0.65; 95% CI: 0.48, 0.87).[123] In contrast, two other sets of investigators performing meta-analyses of randomized placebo-controlled clinical trials concluded that the risks for vertebral and nonvertebral fractures were independent of calcium intake.[124,125]

When the results of 16 observational studies of dietary calcium intake and risk for hip fracture were combined, investigators performing a systematic review of studies on elderly subjects concluded that a significant 4% decrease in the odds of hip fracture accompanied every 300 mg of calcium intake (therefore, population-wide daily dietary consumption of 1200 mg to 1500 mg of elemental calcium should reduce risk for hip fracture by about 15% to 20%).[121] Consistent with the available evidence, the North American Menopause Society, in its 2001 Consensus Opinion, concluded that "Adequate calcium intake (in the presence of adequate vitamin D intake) has been shown to prevent bone loss and reduce fracture risk in peri- and postmenopausal women."[126]

A cost-effectiveness analysis based on published randomized placebo-controlled clinical trials and data from the NHANES III survey concluded that the daily consumption of 1200 mg of supplemental calcium by all individuals over the age of 49 years would prevent 134,764 hip fractures annually, with an associated annual savings of 2.6 billion 1999 dollars in direct medical costs; additional indirect cost savings were not estimated.[118] The daily supplemental consumption of 1200 mg of calcium by all women over the age of 74 years for 3 years would prevent about 27,500 hip fractures annually with a net savings (equal to direct medical costs minus the cost of the supplementation) of about $50.00 per woman.[118] In another analysis, ten years of combined dietary supplementation with calcium (500 to 1000 mg/day) and vitamin D (400 IU/day) in women over 30 years old with osteopenic vertebrae was found to reduce vertebral fracture risk by 30% to 50%, with a net savings of about $500 per fracture avoided.[127] A cost-effectiveness analysis performed in 1996 in France estimated that an annual net savings of FF 150,000,000 could be achieved by supplementing the diets of all elderly women with calcium (1200 mg/day) and vitamin D (800 IU/day).[128] It was estimated that worldwide savings of between 79,000 and 711,000 Euros per 1000 women could be realized from such a supplementation program applied universally.[129] A recent

systematic analysis by The National Coordinating Centre for Health Technology Assessment of the United Kingdom, published in February, 2003, concluded that calcium supplementation is cost-effective after age 60 in preventing vertebral fractures and at all ages in preventing all fractures.[130]

III. Bioavailability of Calcium from the Diet and from Dietary Supplements

Calcium absorption efficiency is fairly similar for most foods, including milk, dairy products and grains.[29] However, the efficiency of calcium absorption is reduced when the food sources include spinach, sweet potatoes, rhubarb, beans, unleavened bread, seeds, nuts, or soy isolates.[29] The fractional absorption of calcium from dietary supplements typically ranges from 25% to 35% (similar to range for calcium in milk).[29] In particular, men and women absorb calcium from calcium citrate and calcium carbonate with equivalent efficiency.[131,132] However, clinical achlorhydria may impair absorption of calcium from calcium carbonate while enhancing the absorption of calcium from calcium citrate.[133]

IV. Amounts of Supplemental Dietary Calcium that Are Effective in Reducing the Risk of Bone Fractures

The reliable and credible scientific literature indicates that daily dietary supplementation with calcium-containing compounds in amounts that provide sufficient elemental calcium to allow individuals to achieve daily total calcium intakes consistent with current Institute of Medicine recommendations for gender, age and reproductive status are effective in reducing the risk of fractures.

Current recommended daily calcium intakes are 800 mg (4 through 8 years old), 1300 mg (9 through 18 years old), 1000 mg (19 through 50 years old) and 1200 mg (over 50 years old).[29] These intakes were chosen in order to ensure maximal skeletal development and duration.[29]

Unfortunately, daily calcium consumption meets or exceeds these amounts in only a small fraction of the population.[29] For example, only half of children 4 to 8 years old consume at least 800 mg of calcium daily; less than 25% of boys 9 to 13 years old consume at least 1300 mg of calcium daily; less than 50% of boys 14 to 18 years old consume at least 1300 mg of calcium daily; only about 5% of adolescent girls consume at least 1300 mg of calcium daily; less than 50% of adult men and only about 10% of adult women consume at least 1000 mg of calcium daily; and less than 10% of the population over 50 years old consumes at least 1200 mg of calcium daily.[29] Recognizing the limitations of any recommendations that rely solely on the implementation of changes in life-long eating and dietary habits, the Institute of Medicine has suggested that "some

seemingly healthy individuals may require higher calcium intakes"[134] and that for individuals at risk for dietary calcium intakes below recommendations, "use of calcium supplements may be desirable in order to meet [recommendations]."[135]

V. Safety of Dietary Supplementation with Calcium in Amounts that Are Effective in Reducing the Risk of Bone Fractures

The US Food and Drug Administration has published its finding that the following calcium-containing compounds are "safe": calcium carbonate, calcium citrate, calcium glycerophosphate, calcium oxide, calcium pantothenate, calcium phosphate, calcium pyrophosphate, calcium chloride, calcium lactate and calcium sulfate.[136,137]

The Tolerable Upper Limit of Intake ("the maximal level of nutrient intake that is unlikely to pose risks of adverse health effects to almost individuals in the target group"[134]) for calcium has been set at 2500 mg daily for males and females over 1 year of age,[29] providing an ample margin of safety for individuals choosing to improve their health by supplementing their diets with calcium. This limit is not set lower during pregnancy or lactation and compares favorably with estimates of daily calcium consumption by modern hunter-gatherers.[13] The Food and Nutrition Board of the Institute of Medicine has stated that "for the majority of the general population, intakes of calcium from food substantially above the UL are probably safe."[29]

No adverse events have occurred when adults with chronic renal failure and receiving hemodialysis have consumed up to 8000 mg of calcium carbonate (providing up to 3200 mg of elemental calcium) daily for up to 48 months[138,139] or when adults with chronic renal failure and not yet receiving hemodialysis have consumed up to 3000 mg of calcium carbonate (providing up to 1200 mg of elemental calcium) daily for 6 months.[140] In these patients, daily dietary supplementation with calcium produced significant improvements in the clinical hyperphosphatemia caused by chronic renal failure.[138-140] In addition, both dialyzed[139] and nondialyzed patients[140] experienced attenuation of disease-induced secondary hyperparathyroidism and bone resorption. Similarly, adults with chronic renal failure and receiving hemodialysis have consumed an unspecified amount of calcium as calcium acetate for 8 weeks with significant improvements in clinical hyperphosphatemia.[141] Boys and girls aged 1 month to 16 years with chronic renal failure and undergoing hemodialysis regularly and consuming 10 to 340 mg of calcium carbonate per kg body weight daily (providing 4 to 136 mg of elemental calcium per kg body weight daily, equivalent to a daily intake of 400 to 13,600 mg of elemental calcium by a 100-kg adult) also have exhibited significantly attenuated hyperphosphatemia and secondary hyperparathyroidism without any adverse reactions.[142]

Increased risk for the development of symptomatic "milk alkali syndrome" (renal impairment, hypercalcemia, alkalosis) may accompany daily intakes of over 4,000 mg of elemental calcium, particularly if accompanied by equivalently large amounts (over 6,000

mg) of carbonate.[143] However, 4 days of daily supplementation with up to 5200 mg of elemental calcium and up to 7800 mg of carbonate was without adverse effect in young adult men and women[144] and 4 months of daily supplementation with 3240 mg of carbonate has been without adverse effect in healthy premenopausal women.[145] Individuals with uremia, hypothyroidism, adrenocortical insufficiency or PTH-secreting tumors may develop clinically relevant hypercalcemia after routine chronic daily consumption of 4,000 mg or more of elemental calcium.[146]

One investigator calculated a Lowest Observed Adverse Effect Level (LOAEL) for calcium for individuals with a history of nephrolithiasis of 1685 mg daily, an amount more than current Institute of Medicine recommendations.[147] The US Food and Drug Administration has concluded that daily intakes of elemental calcium up to at least 1800 mg pose no increased risk for kidney stones among the general population.[137]

A characteristic shared by all of the studies cited in this document is the absolute lack of any reports of any clinically-significant adverse reactions that could be attributed to dietary calcium. As noted by the North American Menopause Society in their 2001 Consensus Opinion, "The side effect profile from recommended levels of calcium intake is insignificant. No calcium intervention trials have reported any serious side effect associated with these levels."[126]

VI. Additional Literature regarding Relationships between Dietary Supplementation with Calcium and Reduction of the Risk of Bone Fractures

This literature review is by necessity brief and targeted to the requirements of the US Food and Drug Administration as concerns a balanced presentation of the published peer-reviewed scientific evidence relevant to the proposed health claims. However, it should be noted that the scientific literature upon which this review relies represents only a small fraction of the total available scientific literature base that may be relevant to the relationships between dietary supplementation with calcium and bone physiology. Literature searches performed on August 26, 2003, on the following topics obtained these numbers of citations:

Calcium and Fractures (2960 citations)
Calcium and Safety (1511 citations)

While there is some (undetermined) degree of repetition in the citations identified by these somewhat related searches, clearly there are at least 3000 unique citations that could be construed to be in some way relevant to this review. After examination of the 4471 citations listed above, 148 were found to be germane to the proposed health claims.

Another literature search performed on August 26, 2003, identified 6542 citations relevant to the topic Calcium and Osteoporosis. However, because the US Food and

Drug Administration ruled on June 22, 1998, that "the term 'risk of fractures' is synonymous with neither osteoporosis nor fractures related to osteoporosis,"[148] these citations were deemed to lack sufficient relevance to be included in this review.

Conclusions

- The amount of ingested calcium that is absorbed increases with increasing daily dietary calcium intake.
- Daily dietary calcium intake of at least 1200 mg of elemental calcium is required in order to maximize the retention of absorbed calcium within the skeleton.
- The amount of dietary calcium required daily in order to maximize calcium retention is approximated by the current Institute of Medicine intake recommendations for this nutrient.
- Maximization of calcium retention is associated with reduced risk of bone fractures.
- At all ages, risk for bone fractures is inversely correlated with daily dietary calcium intakes.
- Daily intakes of calcium that maximize the retention of calcium reduce the risk for bone fractures, including fractures of the hip, vertebrae and wrist.
- Daily intakes of calcium that satisfy the current Institute of Medicine intake recommendations for this nutrient reduce the risk for bone fractures, including fractures of the hip, vertebrae and wrist.
- Routine chronic consumption of dietary and supplemental calcium in amounts consistent with the current Institute of Medicine recommendations for this nutrient is safe.

Summary Conclusions

In conclusion, I find that there is significant scientific agreement in support of the following health claims:

- Calcium may reduce the risk of bone fractures.
- Calcium may reduce the risk of hip fractures.
- Calcium may reduce the risk of vertebral fractures.
- Calcium may reduce the risk of wrist fractures.
- Calcium may reduce the risk of nonvertebral fractures.

/s/ Michael J. Glade[1]

Michael J. Glade, Ph.D., F.A.C.N., C.N.S.

(a copy of my CV is attached)

[1] The original signature page is on file with Emord & Associates, P.C., counsel to Marine Bio Inc. Dr. Glade requested that it not be submitted to FDA to avoid having it posted on the internet and available for nefarious use.

Michael John Glade, Ph.D.

8612 Kedvale Avenue, Skokie IL 60076

TEL: (847)-329-9818 e-mail: the_nutrition_doctor@yahoo.com

EDUCATION:

Ph.D., Animal Science - Nutrition — 1979
Cornell University, Ithaca, New York

Bachelor of Science, Molecular Biology — 1973
Massachusetts Institute of Technology, Cambridge, Massachusetts

PROFESSIONAL AND CAREER OBJECTIVES:

To contribute to the improvement of public health in the areas of nutrition and public health policy through an internationally recognized nutrition program

LICENSES, CERTIFICATIONS, HONORS:

Licensed Dietitian (L.D.), State of Illinois	1995 to present
Certified Nutrition Specialist (C.N.S.)	1993 to present
Fellow, American College of Nutrition (F.A.C.N.)	1992 to present
Honorary Member, Irish Veterinary Medical Association	1988 to present

EXPERIENCE:

Independent Consultant	May 1998 to present
Senior Research Analyst, ECRI, Plymouth Meeting, PA	1997 to 1998
Senior Scientist, American Medical Association, Chicago, IL	1990 to 1997
Visiting Scientist/Research Assistant Professor Northwestern University, Chicago, IL	1986 to 2002
Assistant Professor, University of Maryland, College Park, MD	1981 to 1986
Assistant Professor, Rutgers University, New Brunswick, NJ	1979 to 1981

Director and Nutritionist Adviser to the Board of Directors
International College of Advanced Longevity Medicine 1998 to present

Member, Advisory Board
Society for Integrative Medicine 1998 to present
National Graves' Disease Foundation 1992 to 2001

Recorder
Nutrition Sciences Education and Research Fund 1997 to present

Designated Representative of the C.B.N.S.
Intersociety Physician Nutrition Education Consortium 1996 to present

Policy Paper Reviewer
Council for Agricultural Science and Technology (CAST). 1996 to present

Lecturer
Capital University of Integrative Medicine, Washington, DC 1999 to present
New York Chiropractic College (Diplomate in Nutrition program) 1998 to present
Northwestern University Medical School, Chicago, IL 1990 to 2002

Part-Time Faculty
Biostatistics, University of Bridgeport, Bridgeport, Connecticut 1993 to present

Adjunct Faculty
Union Institute, Cincinnati, Ohio 2000 to present

Book Review Editor
Nutrition: The International Journal of Applied and Basic Nutritional Sciences 1992 to present

Manuscript Reviewer
The Journal of the American Medical Association, The Journal of the American College of Nutrition, Nutrition, and other peer-reviewed journals 1980 to present

Council Coordinator
American College of Nutrition 1994 to 1998

Certification Board for Nutrition Specialists
Director 1992 to present
Director of Educational Programs 2001 to present
President 1996 to 1999
Vice-President 1992 to 1996
Editor, Certifying Examination, Certification Board for Nutrition Specialists 1992 to 2001
Editor/Author
1996 Study Guide for the Certifying Examination for Certified Nutrition Specialists 1996
1996 Candidate's Guide for Licensure as a Nutrition Counselor, State of Illinois 1996
1999 Study Guide for the Certifying Examination for Certified Nutrition Specialists 1999
Study Guide for the Certifying Examination for Certified Nutrition Specialists, 3rd Edition 2002
Lecturer, "Fundamentals of Human Nutrition" Review Course 2002 to present

Complete Nutrition Expertise May 1998 to present

8612 Kedvale Avenue
Skokie IL 60076

- technical support
- educational/promotional materials
- seminars and symposia
- publications
- labeling
- regulatory affairs
- scientific product support
- policy development
- research protocol evaluation
- research design/implementation
- data analysis and interpretation
- product formulation

Product formulation and development projects have emphasized the rational combination of select vitamins, minerals, herbs, and phytonutrients and phytomedicines into formulas for individuals who are attempting to quit smoking or who are afflicted with alcoholism, caffeine dependency, colorectal cancer, breast cancer, cardiovascular disease, osteoporosis, arthritis or celiac disease. These projects have included the assembly of scientific substantiation for both product ingredients and product labeling.

Consulting Clinical Nutritionist September 1999 to present
North Shore Wellness and Cosmetic Surgery
281 Waukegan Road, Northfield, IL 60093

Patient care in the areas of nutritional support for cancer management, restoration of intestinal function, diabetes, chronic fatigue, multiple sclerosis, mental illness, skeletal function, heart disease, chronic fatigue syndrome, fibromyalgia, morbid obesity, yeast infection and smoking cessation.

Nutritionist/Medical Advisor September 2000 to present
Lake County Chapter, Celiac-Sprue Association

Past consulting projects:

Identification and substantiation of structure/function statements for dietary supplements containing ginseng (prepared for a commercial client).

Substantiation of new health claims for dietary supplements containing folic acid (prepared for a petition submitted to the FDA).

Substantiation of new health claims for dietary supplements containing antioxidant vitamins (prepared for petitions submitted to the FDA).

Substantiation of new health claims for dietary supplements containing selenium (prepared for petitions submitted to the FDA).

Substantiation of new health claims for dietary supplements containing antioxidant vitamins (prepared for petitions submitted to the FDA).

Substantiation of new health claims for dietary supplements containing selenium (prepared for petitions submitted to the FDA).

Substantiation of new health claims for dietary supplements containing phosphatidylserine (prepared for petitions submitted to the FDA).

Substantiation of new health claims for dietary supplements containing glucosamine (prepared for petitions submitted to the FDA).

Substantiation of new health claims for dietary supplements containing chondroitin sulfate (prepared for petitions submitted to the FDA).

Design of human trials to demonstrate the safety of a new dietary ingredient (prepared for a commercial client).

Preparation of the scientific background for petitions to FDA requesting approval to import new dietary ingredients (prepared for commercial clients).

Comparison of scientific manuscripts in several copyright infringement cases.

Substantiation of structure/function statements made for several dietary supplements (prepared for commercial clients).

Data analysis for the development of normal reference intervals for a series of new diagnostic tests.

Scientific substantiation and validation of a survey instrument for the assessment of overall health.

Scientific substantiation of a dietary supplement formulation for the support of cognitive functions (prepared for a commercial client).

Evaluation of the safety and effectiveness of a dietary supplement formulation for the chelation of heavy metals (prepared for a commercial client).

Evaluation of the safety and effectiveness of a dietary supplement formulation for enlargement of the human female breast (prepared for a commercial client).

Evaluation of the safety and effectiveness of dietary supplement formulations for enhancement of weight loss (prepared for commercial clients).

Evaluation of the safety and effectiveness of dietary supplement formulations for enhancement of sexual function (prepared for a commercial client).

Evaluation of the safety and effectiveness of dietary supplement formulations for enhancement of immune function (prepared for a commercial client).

Evaluation of the safety and effectiveness of dietary supplement formulations for enhancement of sleep (prepared for a commercial client).

Evaluation of the safety and effectiveness of a dietary supplement formulation for reduction of serum total cholesterol concentration (prepared for a commercial client).

Consultations with the Deputy Commissioner of the Food and Drug Administration concerning the scientific substantiation of proposed health claims for dietary supplements.

Presentations since May 1998:

Herbal management of diabetes. Natural Pharmacy East, Arlington, VA, October 1998.

Nutritional support for breaking nicotine addiction. International College for Advancement of Longevity Medicine Fall Symposium, Reno, NV, October, 1998.

Nutritional support for breaking nicotine addiction. Sixth International Congress of the American Academy of Anti-Aging Medicine, Las Vegas, NV, December, 1998.

Nutritional support for breaking nicotine addiction: A randomized, double-blind, placebo-controlled evaluation of a proprietary dietary supplement. American College of Nutrition Annual Symposium, Washington, DC, October, 1999

Efficacy of an enzyme product derived from *Aspergillus niger* and bromelain (AbsorbAid™) in improving protein absorption in nursing home patients on tube feeding. American College of Nutrition Annual Symposium, Las Vegas, NV, October, 2000.

Preventing cancer with nutrition. Prevention Plus, Oak Park, IL, October, 2000.

Celiac disease. Healthy Eating Seminar Series, Lake County Chapter, Celiac-Sprue Association, Waukegan, IL, October, 2000.

Gluten sensitivity and other digestive disorders. Healthy Eating Seminar Series, Lake County Chapter, Celiac-Sprue Association, Deerfield, IL, January, 2001.

Digestive disease; celiac disease; digestive ecology; using diagnostic technology to target trace elements and vitamin therapy. American Naprapathic Association, Countryside, IL, April 22, 2001.

Biomarkers of aging. Chicagoland Anti-Aging Conference, Wilmette, IL, May 19, 2001.

Restoration of digestive ecology. Designs for Health – Advanced Training in Clinical Nutrition, Designs for Health Institute, Boulder, CO, June 30, 2001.

The relationship between digestive tract function and autism. In-service training, Pfeiffer Foundation, Naperville, IL, July 2001.

Nutrition and brain function. Amer, Naprapathic Assoc., Countryside, IL, April 7,2002.

Fundamentals of Human Nutrition. Two-day Review Course in preparation for the certifying examination of the Certification Board for Nutrition Specialists. American College for the Advancement of Medicine, Ft. Lauderdale, FL, May 15-16, 2002.

Fundamentals of Human Nutrition. Two-day Review Course in preparation for the certifying examination of the Certification Board for Nutrition Specialists. American College of Nutrition, San Antonio, TX, October 2-3, 2002.

Fundamentals of Human Nutrition. Two-day Review Course in preparation for the certifying examination of the Certification Board for Nutrition Specialists. American College of Nutrition, New York, NY. April 5-6, 2003.

Fundamentals of Nutrition. Two-day Review Course in preparation for the certifying examination of the Certification Board for Nutrition Specialists. American College of Nutrition, Miami, FL, April 23-24, 2003.

Upcoming Presentations:

Fundamentals of Human Nutrition. Two-day Review Course in preparation for the certifying examination of the Certification Board for Nutrition Specialists. American College of Nutrition, New York, NY. April 5-6, 2003.

Teaching Lecture Topics since May 1998:

Environmental medicine and detoxification therapy.
Carbohydrate nutrition and nutritional therapy.
Protein nutrition and nutritional therapy.
Nutritional and herbal management of diabetes.
Nutritional therapeutics in cancer.
Nutrition and cancer prevention for consumers.
Celiac disease and its prevention and treatment.
Free radical and antioxidant biology.
Biostatistics for nutritionists (I designed and am teaching this course both in-class and over the internet)

ECRI

5200 Butler Pike, Plymouth Meeting, PA 19462 August 1997 to May 1998

SENIOR RESEARCH ANALYST
Technology Assessment

Evaluation of medical, nutritional, and technological therapies and diagnostic techniques for human endocrine, metabolic, musculoskeletal, and nutritional diseases.

Quality Assurance Manager, National Guidelines Clearinghouse (with AHCPR)

Participant in database design, National Guidelines Clearinghouse (with AHCPR)

Statistical expert, diagnostic technologies and meta-analysis

Provide in-house expertise to ECRI Management on food, device, drug, agriculture and nutrition-related health, policy, legal, and regulatory matters.

SUPERVISOR: Charles Turkelson, Ph.D.
Chief Research Analyst
Technology Assessment
ECRI

AMERICAN MEDICAL ASSOCIATION

515 N. State St. Chicago, IL 60610 1993 to 1997

SENIOR SCIENTIST, Technology Assessment & Nutrition
Department of Technology Assessment

Evaluation of medical, nutritional, and technological therapies and diagnostic techniques for human endocrine, metabolic, musculoskeletal, and nutritional diseases.

Development of Technology Assessments for the AMA *Diagnostic and Therapeutic Technology Assessment (DATTA)* project:

- Diagnostic Value of Plasma Lp(a) Concentrations
- Diagnostic Value of Plasma Apolipoproteins
- Diagnostic Value of Serum Thyroid-Stimulating Hormone (TSH)
- Diagnostic Value of Computerized Dynamic Posturography
- Diagnostic Value of 24-hour Esophageal pH Monitoring
- Therapeutic Value of Peripheral Parenteral Nutrition
- Therapeutic Value of Intraoperative Radiotherapy
- Therapeutic Value of Speech Therapy in Otitis Media
- Therapeutic Value of Recombinant Human Growth Hormone (rhGH) in Children with Short Stature
- Therapeutic Value of Mononuclear Leukocyte ("Buffy Coat") Infusions in Chronic Myelocytic Leukemia
- Therapeutic Value of Medicinal Leeches
- Therapeutic Value of Pedicle Screw Spinal Fixation Systems
- Therapeutic Value of Recombinant Human Growth Hormone (rhGH) in Children with Gonadal Dysgenesis

Related Duties:

Statistician; perform statistical analyses for all physician surveys administered by the *DATTA* project.

Co-Editor of the monthly AMA newsletter, *Technology News*.

Provide in-house expertise to AMA Senior Management on food, device, drug, agriculture and nutrition-related health, policy, legal, and regulatory matters.

Secretary, AMA House of Delegates Reference Committee E (advise AMA policy committees on medicine, nutrition, and public health).

Publications:

Published In:	No. of Publications:
DATTA Assessments:	13
peer-reviewed journals:	4
Proceedings chapters:	4
book reviews:	11
general public press:	16
peer-reviewed journals (submitted):	5

Original articles published in the monthly AMA newsletter, *Technology News*:

Risk Assessment in the Establishment of Upper Safe Limits for Nutrient Intakes	12/96
Dietary Fat and Cancer: Molecular Mechanisms	10/96
Clinical Significance of Melatonin (with B. Kendler)	9/96
Designing, Testing, and Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities	6/96
Dietary Phytochemicals in Cancer Prevention and Treatment	11/95
Electromagnetic Compatibility for Medical Devices: Issues and Solutions	9/95
FDA/NIH-Sponsored Conference: Comparing Treatments: Safety, Effectiveness, and Cost-Effectiveness	5/95
Clinical Significance of Oxidative Stress (with B. Kendler)	11/95
Diet and Cancer: Molecular Mechanisms of Interactions	1-2/95
Management of Disorders of Cholesterol, Triglyceride, and Lipoprotein Metabolism	11/94
AMA Annual Meeting Update (with S. Kalousdian)	7-8/94
Drug and Device-Induced Disease: Developing a Blueprint for the Future	/94
AMA Interim Meeting Update (with S. Kalousdian)	1-2/94
AMA Annual Meeting Update (with S. Kalousdian)	8/93
Breast Cancer Risk and Diet	1/93

Author of AMA policy statements on nutrition issues:

food irradiation;

lipoproteinemia;

bacterial contamination of meat;

dietary calcium requirements;

folic acid supplementation to prevent neural tube defects;

thiamin supplementation of alcoholic beverages to prevent polyneuropathy;

neonatal hyponatremia from hypo-osmolar bottled water

Speaking Invitations:

The Dietary Supplement and Health Education Act of 1994. Annual Meeting of the American College of Nutrition, Washington, DC, October, 1995.

Innovation in clinical nutrition. Harvard University, May 6, 1995.

Environmental medicine. New York Chiropractic College, April 29, 1995.

Environmental medicine. New York Chiropractic College, September 11, 1994.

Additional Responsibilities:

Meeting with representatives of the Food and Drug Administration, the US Department of Agriculture, and other federal agencies concerning:

food, device and drug regulation;

food safety;

direct to consumer advertising of medical therapies.

Collaboration with other AMA staff in the development of scripts for television programs aired on American Medical Television.

Represented AMA on "National Educational Forum on Food Safety Issues."

Book Review Editor, *Nutrition: The International Journal of Applied and Basic Nutritional Sciences.*

Reviewed manuscripts submitted to *the Journal of the American Medical Association*, *the Journal of the American College of Nutrition*, and other peer-reviewed journals.

Reviewed advertisements intended for use in AMA publications.

Policy paper reviewer for the Council for Agricultural Science and Technology (CAST).

Invitations to Chair National Meetings:

Invited to chair and organize a session on "Nutritional Controversies" at the 1996 Annual Meeting of the American College of Nutrition, San Francisco.

Invited to serve as co-chairman of a session of the 1994 Malnutrition and AIDS Symposium, Los Angeles.

Invited to serve as co-chairman of a session of the 1994 Annual Meeting of the American College of Nutrition, Atlanta.

SUPERVISOR: Sona Kalousdian, MD, MPH
Department Director, Department of Technology Assessment
American Medical Association
(773) 384-4915

AMERICAN MEDICAL ASSOCIATION

515 N. State St. Chicago, IL 60610 1990 to 1993

SENIOR SCIENTIST, Endocrinology, Metabolism & Nutrition
Department of Drugs

Evaluation of medical and nutritional therapies and diagnostic techniques for human endocrine, metabolic, musculoskeletal, and nutritional diseases.

Extensive revision of chapters in the Congressionally-recognized compendium of FDA-approved unlabeled drug use and nutritional therapy, *AMA Drug Evaluations*:

Fluid, Electrolyte, and Acid-Base Therapy (pp. 865-880*)
Drugs Used for Urolithiasis (pp. 907-924)
Drugs Used in Adrenocortical Dysfunction (pp. 1017-1036)
Drugs Used in Thyroid Disease (pp. 1037-1062)
Vitamins and Minerals (pp. 2283-2306)
Parenteral and Enteral Nutrition (pp. 2307-2362)
Drugs Used in Obesity (pp. 2439-2454)
Treatment of Disorders of Cholesterol and Lipoprotein Metabolism (pp. 2455-2500)

(* page numbers as in the 1995 edition)

Assistant Secretary, AMA House of Delegates Reference Committee E (advise AMA policy committees during development of policies concerning medicine, nutrition, and public health).

Collaboration with other AMA staff in the development of scripts for television programs aired on American Medical Television

Publications:

Published In:	No. of Publications:
AMA Drug Evaluations Chapters:	8
peer-reviewed journals:	12
Proceedings chapters:	6
book reviews:	1
general public press:	6

Speaking Invitations:

A review of hormonal regulation of cartilage growth in foals. Symposium on Equine Osteochondrosis, Cambridge University, United Kingdom, September, 1992.

Marginal copper deficiency as a cause of defective angiogenesis in chondrodysplasia. Symposium on Equine Osteochondrosis, Cambridge University, United Kingdom, September, 1992.

Endocrine regulation of equine growth plate chondrocytes. Symposium on Equine Osteochondrosis, Cambridge University, United Kingdom, September, 1992.

Equine osteochondrosis as a manifestation of induced episodic "pseudohypothyroidism." Symposium on Equine Osteochondrosis, Cambridge University, United Kingdom, September, 1992.

Insulin and thyroid hormones influence matrix production by chondrocytes. Seminars in Endocrinology, Northwestern University, Chicago, IL, April 2, 1991.

Additional Responsibilities:

Meetings with representatives of the Food and Drug Administration, the US Department of Agriculture, and other federal agencies concerning:

food, device and drug regulation;

food safety;

direct to consumer advertising of medical therapies

Collaboration with Centers for Disease Control in development of recommendations concerning folic acid and the prevention of neural tube defects (*Morbidity and Mortality Weekly*, August 2, 1991, and September 21, 1992).

Author of AMA policy statement on monosodium glutamate.

Provide in-house expertise to AMA Senior Management on food, device, drug, agriculture and nutrition-related health, policy, legal, and regulatory matters.

Represented AMA on "National Educational Forum on Food Safety Issues".

Book Review Editor, *Nutrition: The International Journal of Applied and Basic Nutritional Sciences.*

Review manuscripts submitted to *the Journal of the American Medical Association*, *the Journal of the American College of Nutrition*, and other peer-reviewed journals.

Review advertisements intended for use in AMA publications.

Coordinator, Council on Endocrinology, Bone, and Minerals; American College of Nutrition.

Advisory Board Member, National Graves' Disease Foundation

SUPERVISOR: Joseph Cranston, Ph.D.
Department Director
Department of Drugs
American Medical Association

NORTHWESTERN UNIVERSITY

303 E. Chicago Avenue, Chicago, IL 60610 1986 to 1990

RESEARCH ASSISTANT PROFESSOR
Department of Pharmacology

Funded originally as an NIH Senior Fellowship, this position - including both research and teaching - has been continued on a part-time, unpaid basis through the present time as a Visiting Scientist, Department of Molecular Pharmacology and Biological Chemistry

Laboratory and field research; presentation and publication of research findings; fund raising; maintenance of laboratory; practice of safe and proper animal housing and handling; practice of safe handling of hazardous substances.

Concentration on the effects of nutrients, hormones and growth factors on skeletal development and disease.

Guest lectures on pancreatic and thyroid disease and their prevention and medical and nutritional management.

Publications:

Published In:	No. of Publications:
peer-reviewed journals:	11
Proceedings chapters:	8
abstracts:	4
general public press:	98

Speaking Invitations:

Response of arthritic chondrocytes to polysulfated glycosaminoglycans. Skeletal Biology Program, Case Western Reserve University, Cleveland OH, May 14, 1990.

Flora and fauna of Africa and Europe. Department of Pharmacology, Northwestern University, Chicago, IL, February 9, 1989.

Influences of diet and endocrinology on equine developmental orthopedic disease. Department of Animal Sciences, University of Guelph, Ontario, Canada, January 18, 1989.

Diet and growth quality. Equine management class, University of Guelph, Ontario, Canada, January 18, 1989.

Fermentation enhancers. Department of Animal Sciences, University of Guelph, Ontario, Canada, January 17, 1989.

Nitrogen metabolism in the equine. Equine management class, University of Guelph, Ontario, Canada, January 16, 1989.

Feeding and management of pleasure and show horses. Potomac Horse Club, Silver Spring, MD, October, 1988.

Feeding and management of pleasure and show horses. Potomac Horse Club, Silver Spring, MD, October, 1988.

Homeorrhesis and the growing animal. Biological Sciences Seminar, University College, Dublin, Ireland, October 17, 1988.

Nutrition and developmental disorders of equidae. Department of Zoology, University College, Dublin, Ireland, October 17, 1988.

Nitrogen metabolism in horses. Veterinary College of Ireland, Dublin, Ireland, October 14, 1988.

The role of yeast culture in the nutritional management of young horses. 100th Irish Veterinary Congress, Dublin, Ireland, September 23, 1988.

The role of endocrine factors in equine developmental orthopedic disease. Developmental Orthopedic Disease Panel, American Association of Equine Practitioners Annual Meeting, New Orleans, LA, November 29, 1987.

Diet, chondrodysplasias and animals. Oral Biology Seminar, Northwestern University, Chicago, IL, October 29, 1987.

Effects of yeast culture on nitrogen metabolism in young horses. Alltech Biotechnology Symposium, Lexington, KY, April, 1987.

Bibliometric analysis of research activity in Brazil. Central Intelligence Agency, MacClean, VA, March, 1987.

Bibliometric analysis of research activity in Spain. Ministry of Science and Education, Madrid, Spain, March, 1987.

Cartilage disorders associated with changes in thyroid hormone metabolism. The Chicago Endocrine Society, Chicago, IL, December, 1986.

Dietary causes of osteochondrosis. Pathology Seminar, Northwestern University, Chicago, IL, April, 1986.

UNIVERSITY OF MARYLAND

College Park, Maryland 1981 to 1986

ASSISTANT PROFESSOR, Department of Animal Sciences
College of Agricultural Sciences

Teaching: (Class, laboratory, barn; lecture, hands-on formats)

Animal Husbandry (nutrition, diet formulation, diseases, management, genetics, physiology, functional morphology)

Animal Training (including principles of animal behavior and their application to training)

Safe Animal Handling (including principles of animal behavior and their application to safe practices in handling animals)

Protein Nutrition (graduate course)

Training:

How to Teach and Supervise Animal Training (undergraduate and graduate students; written materials; videotapes)

Laboratory Techniques (undergraduate and graduate students)

Field Research Techniques (undergraduates and graduates)

Dissertation and Scientific Writing

Grant Proposal Preparation

Research:

Animal Nutrition and Physiology Projects, including several in collaboration with the National Zoo, Washington, DC

Publications:

Published In:	No. of Publications:
peer-reviewed journals:	17
Proceedings chapters:	8
abstracts:	8
general public press:	73

Other projects: (in addition to those documented in publications)

hormone secretion rates in pigs

skeletal growth in monkeys

pharmacokinetics of ivermectin in bullfrogs

growth hormone concentrations in horses and zebras

Invitation to Chair National Meeting:

Invited to serve as co-chairman of a Non-Ruminant Nutrition session at the 1982 meeting of the American Society of Animal Science, Guelph, Ontario, Canada.

Speaking Invitations:

Quality feed management: tips for proper production and storage. Baltimore Horse Seminar, March, 1985.

Dietary carbohydrate induction of the multiple-messenger, inositol-calmodulin pathway. Animal Sciences Seminar, University of Maryland, February, 1985.

The use of ultrasound to monitor neonatal bone development. Invited seminar, Walter Reed Medical Center, Washington, DC, December, 1984.

Mechanisms of dietary induction of osteochondrosis. Invited seminar, Department of Animal Science, University of Alberta, Edmonton, Canada, August, 1984.

The Use of Self-Supervised Activity to Acquaint College Students with the Teacher-Student Dynamic. 10th International Conference, Improving University Teaching, College Park, MD, July, 1984.

Diagnostic ultrasound - a non-invasive method for examining bone. Pediatric Research Conference, University of Maryland School of Medicine, May, 1984.

Electrical stimulation of bone healing. Alice Deal Science Day, May, 1984.

Non-Traditional feeding practices for the performance horse. Maryland Nutrition Conference, Baltimore, MD, March, 1984.

The use of ultrasound. Nutritional Sciences Colloquium, University of Maryland, February, 1984.

Nutrient-hormone interactions and their impact on growth. Nutritional Sciences Colloquium, University of Maryland, February, 1984.

Feeding horses for a lot less money. Eastern Amateur Arabian Horse Show Circuit Fall Meeting, December, 1983.

Equine nutritional requirements. Baltimore Horse Seminar, November, 1983.

The costs of owning a horse, Maryland Society for the Prevention of Cruelty to Animals Field Day, May, 1983.

Ultrasonic measurement of bone strength. Alice Deal Science Day, April, 1983.

Nutritional manipulation of bone and joint development in growing horses. Maryland Nutrition Conference, Washington, DC, March, 1982.

Developmental origins of growth abnormalities. Animal Sciences Seminar, University of Maryland, October, 1981.

Additional Responsibilities:

Design of Animal Habitats:

Personally redesigned three multi-acre animal housing facilities, and assisted in their physical renovation

Animal Care:

Collaboration with veterinarians in prophylactic and interventive medical care, including personally:

administering medications by mouth
injection (intramuscular; intravenous)
nasogastric intubation; rectal gavage
bandaging; suturing
development of growth plate biopsy procedure for ungulates
necropsy

Animal Management:

Directly responsible for the management, breeding, and training of up to 120 horses residing at multi-building and multi-site facilities whose activities encompassed teaching, research, breeding, continuing adult education, veterinary care, demonstrations

Supervision of Personnel:

Supervision of up to two dozen permanent and temporary full and part time employees and volunteers engaged in animal husbandry

Record Keeping; Budgets:

Directly responsible for planning, developing, administering, and adhering to expense and revenue budgets, and for extensive and comprehensive record-keeping concerning all facets of a major university equine program

Fund-Raising:

Obtaining funds to support all programs and activities

Sources included federal agencies, state agencies, private foundations, private individuals, corporate entities, animal sales, animal rental

RUTGERS UNIVERSITY

New Brunswick, NJ 1979 to 1981

ASSISTANT PROFESSOR, Department of Animal Sciences

Teaching: (Class, laboratory, barn; lecture, hands-on formats):

Animal Husbandry (nutrition, diet formulation, diseases, management, genetics, physiology, functional morphology)

Animal Training (including principles of animal behavior and their application to training)

Safe Animal Handling (including principles of animal behavior and their application to safe practices in handling animals)

Training:

Field Research Techniques (undergraduates and graduates)

Grant Proposal Preparation

Research:

Animal Nutrition and Physiology Projects

Publications:

Published In:	No. of Publications:
Proceedings chapters	1
abstracts	1

Speaking Invitations:

Digestive physiology of the horse. Animal Sciences Seminar, University of Maryland, September, 1980.

Similarities between effects of dexamethasone on growing cartilage and osteochondrosis dissecans. Animal Science Seminar, University of California at Davis, April, 1980.

Osteochondrosis dissecans and growth suppression in dexamethasone treated horse foals. American Association of Equine Practitioners Annual Meeting, Miami Beach, December, 1979.

Effects of dexamethasone on calcium metabolism of pony foals. Animal Sciences Seminar, Rutgers University, May, 1979.

Additional Responsibilities:

Design of Animal Habitats:

Personally redesigned a multi-acre animal housing facility, and assisted in its physical renovation

Animal Care:

Collaboration with veterinarians in prophylactic and interventive medical care, including personally:

administering medications by mouth
injection (intramuscular; intravenous)
nasogastric intubation; rectal gavage
bandaging; suturing; necropsy

Animal Management:

Directly responsible for the management, breeding, and training of up to 11 horses residing at multi-building and multi-site facilities whose activities encompassed teaching, research, continuing adult education, veterinary care, demonstrations

Supervision of Personnel:

Directly responsible for the supervision of two permanent part time employees and a dozen or so volunteers engaged in animal husbandry

Record Keeping; Budgets:

Directly responsible for planning, developing, administering, and adhering to expense and revenue budgets, and for extensive and comprehensive record-keeping concerning all facets of a major university equine program

Fund-Raising:

Obtaining funds to support all programs and activities

Sources included federal agencies, state agencies, private foundations, private individuals, corporate entities, animal sales, animal rental

Refereed Journal Articles:

1. Glade, M.J. The effects of gestation, lactation, yeast culture and maternal calcium intake on the mechanical strength of equine bone. *Journal of Equine Veterinary Science*: submitted for publication.

2. Heimburger, D.C., and the Intersociety Professional Nutrition Education Consortium. 2002. Training and certifying gastroenterologists as Physician Nutrition Specialists. *Journal of Clinical Gastroenterology* 34:505-508.

3. Glade, M.J., D. Kendra and M.V. Kaminski, Jr. 2001. Improvement in protein utilization in nursing-home patients on tube feeding supplemented with an enzyme product derived from *Aspergillus niger* and bromelain. *Nutrition* 17:348-350.

4. Heimburger, D.C., and the Intersociety Professional Nutrition Education Consortium. 2000. Physician-nutrition-specialist track: If we build it, will they come? *American Journal of Clinical Nutrition* 71:1048-1053.

5. Glade, M.J. 1997. Intake of dietary calcium to reduce the incidence of osteoporosis. *Archives of Family Medicine* 6:491-494.

6. Glade, M.J. 1995. Management of disorders of cholesterol, triglyceride, and lipoprotein metabolism. *Archives of Family Medicine* 4:869-878.

7. Glade, M.J. 1995. Continuous ambulatory esophageal pH monitoring. *Journal of the American Medical Association* 274:662-668.

8. Glade, M.J., Y.S. Kanwar and P.H. Stern. 1994. Insulin and thyroid hormones alter chondrocyte metabolism in cell culture independently and in combination. *Connective Tissue Research* 31:37-44.

9. Glade, M.J. 1993. The effects of gestation, lactation, and maternal calcium intake on the mechanical strength of equine bone. *Journal of the American College of Nutrition* 12:372-377.

10. Glade, M.J. 1992. Effects of Yucca shidigera extract on feed utilization by equine weanlings. *Journal of Equine Veterinary Science* 12:93-98.

11. Letcher, J. and M.J. Glade. 1992. Efficacy of ivermectin as an anthelmintic in leopard frogs. *Journal of the American Veterinary Medical Association* 200:537-538.

12. Glade, M.J., Y.S Kanwar and T.J. Hefley. 1991. Enzymatic isolation of chondrocytes from immature rabbit articular cartilage and their maintenance of phenotypic expression in culture. *Journal of Bone and Mineral Research* 6:217-226.

13. Glade, M.J. 1991. Timed administration of leucine, isoleucine, valine, glutamine, and carnitine to enhance athletic performance. *Equine Athlete* 4:1-10.

14. Glade, M.J. 1991. Effects of dietary yeast culture supplementation of lactating mares on the digestibility and retention of the nutrients delivered to nursing foals via milk. *Journal of Equine Veterinary Science* 11:323-329.

15. Glade, M.J. 1991. Dietary yeast culture supplementation of mares during late gestation and early lactation. 3. Effects on mare and foal plasma metabolite, amino acid and endocrine profiles. *Journal of Equine Veterinary Science* 11:167-175.

16. Glade, M.J. 1991. Dietary yeast culture supplementation of mares during late gestation and early lactation. 2. Effects on milk production, milk composition, weight gain and linear growth of nursling foals. *Journal of Equine Veterinary Science* 11:89-95.

17. Glade, M.J. 1991. Dietary yeast culture supplementation of mares during late gestation and early lactation. 1. Effects on dietary nutrient digestibilities and fecal nitrogen partitioning. *Journal of Equine Veterinary Science* 11:10-16.

18. Glade, M.J. and M.D. Sist. 1990. Supplemental yeast culture alters the plasma amino acid profiles of nursling and weanling horses. *Journal of Equine Veterinary Science* 10:369-379.

19. Glade, M.J. and N.K. Luba. 1990. Benefits to foals of feeding soybean meal to lactating broodmares. *Journal of Equine Veterinary Science* 10:422-428.

20. Glade, M.J. and M. Campbell-Taylor. 1990. Effects of dietary yeast culture supplementation during the conditioning period on equine exercise physiology. *Journal of Equine Veterinary Science* 10:434-443.

21. Glade, M.J. 1990. Polysulfated glycosaminoglycan (PSGAG) accelerates the synthesis of collagen and glycosanminoglycans by arthritic equine cartilage tissues and chondrocytes. *American Journal of Veterinary Research* 51:779-785.

22. Sist, M.D., Youngblood, M.A., Williams, J.F. and Glade, M.J. 1988. Salivary and serum estrone sulfate levels in pregnant mares. *Journal of Equine Veterinary Science* 8: 164-167.

23. Glade, M.J. and M.D. Sist. 1988. Dietary yeast culture supplementation enhances urea recycling in the equine large intestine. *Nutrition Reports International* 37: 11-19.

24. Wright, L.L., M.J. Glade and J. Gopal. 1987. The use of transmission ultrasonics to assess bone status in the human newborn. *Pediatrics Research* 22:541-544.

25. Glade, M.J. and N.K. Luba. 1987. Serum triiodothyronine and thyroxine concentrations in weanling horses fed carbohydrate by direct gastric infusion. *American Journal of Veterinary Research* 48:578-582.

26. Glade, M.J., N.K. Luba, and H.F. Schryver. 1986. Effects of age and diet on the development of mechanical strength by the cannon bones of young horses. *Journal of Animal Science* 63:1432-1444.

27. Glade, M.J. and L.M. Biesik. 1986. Changes in serum hormone concentrations in weanling horses following gastric infusion of sucrose or casein. *Nutrition Reports International* 33:651-659.

28. Glade, M.J. and L.M. Biesik. 1986. Enhanced nitrogen retention in yearling horses supplemented with yeast culture. *Journal of Animal Science* 62:1633-1640.

29. Glade, M.J. 1986. Estimation of urine flow rate in weanling and yearling horses. *American Journal of Veterinary Research* 47:2151-2156.

30. Glade, M.J. and T.H. Belling. 1986. A dietary etiology for osteochondrotic cartilage. *Journal of Equine Veterinary Science* 6:151-154.

31. Glade, M.J. 1986. The control of cartilage growth in osteochondrosis. *Journal of Equine Veterinary Science* 6:175-187.

32. Glade, M.J. 1986. "Social Sleeping" among confined horses. *Journal of Equine Veterinary Science* 6:155-157.

33. Glade, M.J. and R.A. Salzman. 1985. Effects of hoof angulation on hoof growth and contraction in the horse. *Journal of Equine Veterinary Science* 5:45-50.

34. Glade, M.J. and T.J. Reimers. 1985. Effects of dietary energy supply on serum thyroxine, tri-iodothyronine and insulin concentrations in young horses. *Journal of Endocrinology* 104:93-98.

35. Glade, M.J., D. Beller, J. Bergen, D. Berry, E. Blonder, J. Bradley, M. Cupelo and J. Dallas. 1985. Dietary protein in excess of requirements inhibits renal calcium and phosphorus reabsorption in young horses. *Nutrition Reports International* 31:649-659.

36. Glade, M.J. 1985. Stimulation of electromagnetic osteogenesis in healthy growing yearlings. *Journal of Equine Veterinary Science* 5:149-153.

37. Glade, M.J. 1985. Overfeeding energy to horses. *Journal of Equine Veterinary Science* 5:95.

38. Glade, M.J., S. Gupta and T.J. Reimers. 1984. Hormonal responses to high and low planes of nutrition in weanling Thoroughbreds. *Journal of Animal Science* 59:658-665.

39. Glade, M.J. and T.H. Belling. 1984. Growth plate cartilage metabolism, morphology and biochemical composition in over- and underfed horses. *Growth* 48:473-482.

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41. Glade, M.J. 1984. "Social sleeping" behavior in young horses. *Equine Practice* 6:10-14.

42. Glade, M.J. 1984. The influence of dietary fiber digestibility on the nitrogen requirements of mature horses. *Journal of Animal Science* 58:638-646.

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46. Glade, M.J., L. Krook, H.F. Schryver and H.F. Hintz. 1982. Morphologic and biochemical changes in cartilage of foals treated with dexamethasone. *Cornell Veterinarian* 73:170-192.

47. Glade, M.J., L. Krook, H.F. Schryver and H.F. Hintz. 1982. Calcium metabolism in glucocorticoid-treated foals. *Journal of Nutrition* 112:67-76.

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1. Glade, M.J., Kendra, D., Kaminsky, M.V., Jr. 2000. Efficacy of an enzyme product derived from *Aspergillus niger* and bromelain (AbsorbAid™) in improving protein absorption in nursing home patients on tube feeding. *Proceedings, Annual Meeting of the American College of Nutrition*, Las Vegas, NV, October.

2. Heimburger, D., and IPNEC. 2000. Training the Physician Nutrition Specialist (PNS). *Proceedings, Annual Meeting of the American College of Nutrition*, Las Vegas, NV, October.

3. Glade, M.J. 1998. Nutritional support for breaking nicotine addiction. *Proceedings, Sixth International Congress on Anti-Aging and Biomedical Technologies* (American Academy of Anti-Aging Medicine), Las Vegas, NV, December, p. unpaged.

4. Glade, M.J. 1998. Nutritional support for breaking nicotine addiction. *Proceedings, International College for Advancement of Longevity Medicine Fall Symposium,* Reno, NV, October, unpaged.

5. Glade, M.J. 1998. Herbal management of diabetes. *Proceedings, Second Annual Natural Pharmacy East Conference,* Arlington, VA, October, unpaged.

6. Glade, M.J., and M.E. Allen. 1996. Assessment of skeletal development in leopard geckos. II. Long bone morphometry and breaking strength. *Proceedings, Ninth Dr. Scholl Nutrition Conference,* Chicago, IL, October, unpaged.

7. Glade, M.J. 1995. The Dietary Supplement and Health Education Act of 1994. *Proceedings, Annual Meeting of the American College of Nutrition*, Washington, DC, October, p. 557.

8. Glade, M.J. 1993. $CuSO_4$ and chelated copper are bioequivalent when added to the diets of nursing foals. *Proceedings, Annual Meeting of the American College of Nutrition*, Chicago, October, p. 589.

9. Glade, M.J. 1993. $CuSO_4$ and chelated copper are bioequivalent when added to the culture medium of cartilage tissue and cells. *Proceedings, Annual Meeting of the American College of Nutrition*, Chicago, October, p. 589.

10. Glade, M.J. 1992. Equine osteochondrosis as a manifestation of induced episodic "pseudohypothyroidism." *Proceedings, Symposium on Equine Osteochondrosis*, Cambridge University, United Kingdom, September, p. 44.

11. Glade, M.J. 1992. Endocrine regulation of equine growth plate chondrocytes. *Proceedings, Symposium on Equine Osteochondrosis*, Cambridge University, United Kingdom, September, pp. 42-43.

12. Glade, M.J. 1992. Marginal copper deficiency as a cause of defective angiogenesis in chondrodysplasia. *Proceedings, Symposium on Equine Osteochondrosis*, Cambridge University, United Kingdom, September, pp. 30-31.

13. Glade, M.J. 1992. A review of hormonal regulation of cartilage growth in foals. *Proceedings, Symposium on Equine Osteochondrosis*, Cambridge University, United Kingdom, September, pp. 19-20.

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15. Glade, M.J. 1992. Marginal copper deficiency as a cause of defective angiogenesis in chondrodysplasia. *Proceedings, Annual Meeting of the American College of Nutrition*, San Diego, October, p. 600.

16. Glade, M.J., C. Cahill and M. Campbell. 1989. Effect of exercise on plasma growth hormone concentrations in foals. *Proceedings, Equine Nutrition and Physiology Society*, pp. 63-64.

17. Glade, M.J. 1989. Effects of specific amino acid supplementation on lactic acid production by horses exercised on a treadmill. *Proceedings, Equine Nutrition and Physiology Society*, pp. 244-251.

18. Glade, M.J. 1989. Undergraduates and publishable equine research. *Proceedings, Equine Nutrition and Physiology Society*, pp. 233-235.

19. Glade, M.J. 1989. Supplemental yeast culture alters the plasma amino acid profiles of weanling Quarter horses. *Proceedings, Equine Nutrition and Physiology Society*, pp. 119-123.

20. Campbell, M. and M.J. Glade. 1989. Effects of dietary yeast culture supplementation during the conditioning period on heart rates and lactic acid production by horses exercised on a treadmill. *Proceedings, Equine Nutrition and Physiology Society*, pp. 72-78.

21. Glade, M.J. and P.H. Stern. 1988. Effect of polysulfated glycosaminoglycan (PSGAG) on monolayer cultures of articular chondrocytes. *Journal of Bone and Mineral Research*: 3: Suppl. 1:465.

22. Glade, M.J. 1988. The role of endocrine factors in equine developmental orthopedic disease. *American Association of Equine Practitioners* 33:171-189.

23. Wright, L.L., M.J. Glade and J. Gopal. 1987. Transmission ultrasonics to assess bone status in the human newborn. *Pediatrics Research*: 21:440A.

24. Glade, M.J. and N.K. Luba. 1987. Benefits to foals of feeding soybean meal to lactating broodmares. *Proceedings, Equine Nutrition and Physiology Society*, pp. 593-598.

25. Glade, M.J., T.J. Hefley and P.H. Stern. 1987. A cartilage digestion method maximizing digestion rates and cell yields. *Journal of Bone and Mineral Research*: 2: Suppl. 1: Abstr. 422.

26. Glade, M.J. 1987. The development of mechanical strength in the radius and ulna of the juvenile rhesus monkey. *Journal of Bone and Mineral Research*: 2: Suppl. 1: Abstr. 355.

27. Glade, M.J. 1987. Cross-sectional geometry of equine metacarpal bones: an initial biomechanical investigation. *Proceedings, Equine Nutrition and Physiology Society*, pp. 537-544.

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34. Glade, M.J. and N.K. Luba. 1984. Maximum cannon bone breaking strength is not increased by overfeeding young horses. *Journal of Animal Science*: 59:Abstr. 171.

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36. Glade, M.J. 1984. Insulin and thyroxine responses to high energy and protein feeding of weanling horses. *Journal of Animal Science*: 59:Abstr. 476.

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38. Gupta, S. and M.J. Glade. 1983. Hormonal responses to high and low planes of nutrition in weanling Thoroughbreds. *Proceedings, Equine Nutriton and Physiology Society*, pp. 45-49.

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LITERATURE CITED *for Calcium and Bone Fractures Health Claims*

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